

Met	Asp	Trp	Pro	His	Asn	Leu	Leu	Phe	Leu	Leu	Thr	Ile	Ser	Ile	
1					5				10						15
Phe	Leu	Gly	Leu	Gly	Gln	Pro	Arg	Ser	Pro	Lys	Ser	Lys	Arg	Lys	
				20					25					30	
Gly	Gln	Gly	Arg	Pro	Gly	Pro	Leu	Ala	Pro	Gly	Pro	His	Gln	Val	
				35					40					45	
Pro	Leu	Asp	Leu	Val	Ser	Arg	Met	Lys	Pro	Tyr	Ala	Arg	Met	Glu	
				50					55					60	
Glu	Tyr	Glu	Arg	Asn	Ile	Glu	Glu	Met	Val	Ala	Gln	Leu	Arg	Asn	
				65					70					75	
Ser	Ser	Glu	Leu	Ala	Gln	Arg	Lys	Cys	Glu	Val	Asn	Leu	Gln	Leu	
				80					85					90	
Trp	Met	Ser	Asn	Lys	Arg	Ser	Leu	Ser	Pro	Trp	Gly	Tyr	Ser	Ile	
				95					100					105	
Asn	His	Asp	Pro	Ser	Arg	Ile	Pro	Val	Asp	Leu	Pro	Glu	Ala	Arg	
				110					115					120	
Cys	Leu	Cys	Leu	Gly	Cys	Val	Asn	Pro	Phe	Thr	Met	Gln	Glu	Asp	
				125					130					135	
Arg	Ser	Met	Val	Ser	Val	Pro	Val	Phe	Ser	Gln	Val	Pro	Val	Arg	
				140					145					150	
Arg	Arg	Leu	Cys	Pro	Pro	Pro	Pro	Arg	Thr	Gly	Pro	Cys	Arg	Gln	
				155					160					165	
Arg	Ala	Val	Met	Glu	Thr	Ile	Ala	Val	Gly	Cys	Thr	Cys	Ile	Phe	
				170					175					180	

FIGURE 1

aggcgggag cagctgcagg ctgaccttgc agcttggcgg aatggactgg 50
 cctcacaacc tgctgtttct tcttaccatt tccatcttcc tggggctggg 100
 ccagcccagg agccccaaaa gcaagaggaa ggggcaaggg cggcctgggc 150
 ccctggcccc tggccctcac caggtgccac tggacctggt gtcacggatg 200
 aaaccgtatg cccgcatgga ggagtatgag aggaacatcg aggagatggt 250
 ggcccagctg aggaacagct cagagctggc ccagagaaaag tgtgaggtca 300
 acttgcagct gtggatgtcc aacaagagga gcctgtctcc ctggggctac 350
 agcatcaacc acgaccccag ccgtatcccc gtggacctgc cggaggcacg 400
 gtgcctgtgt ctgggctgtg tgaaccctt caccatgcag gaggaccgca 450
 gcatggtgag cgtgccggtg ttcagccagg ttctgtgcg ccgccgcctc 500
 tgcccgccac cgcgccgcac agggccttgc cgcagcgcg cagtcatgga 550
 gaccatcgt gtgggctgca cctgcatctt ctgaatcacc tggcccagaa 600
 gccaggccag cagcccagaa ccacctcct tgcacctttg tgccaagaaa 650
 ggccatgaa aagtaaacac tgacttttga aagcaag 687

FIGURE 2

Met	Thr	Leu	Leu	Pro	Gly	Leu	Leu	Phe	Leu	Thr	Trp	Leu	His	Thr	1	5	10	15
Cys	Leu	Ala	His	His	Asp	Pro	Ser	Leu	Arg	Gly	His	Pro	His	Ser	20	25	30	
His	Gly	Thr	Pro	His	Cys	Tyr	Ser	Ala	Glu	Glu	Leu	Pro	Leu	Gly	35	40	45	
Gln	Ala	Pro	Pro	His	Leu	Leu	Ala	Arg	Gly	Ala	Lys	Trp	Gly	Gln	50	55	60	
Ala	Leu	Pro	Val	Ala	Leu	Val	Ser	Ser	Leu	Glu	Ala	Ala	Ser	His	65	70	75	
Arg	Gly	Arg	His	Glu	Arg	Pro	Ser	Ala	Thr	Thr	Gln	Cys	Pro	Val	80	85	90	
Leu	Arg	Pro	Glu	Glu	Val	Leu	Glu	Ala	Asp	Thr	His	Gln	Arg	Ser	95	100	105	
Ile	Ser	Pro	Trp	Arg	Tyr	Arg	Val	Asp	Thr	Asp	Glu	Asp	Arg	Tyr	110	115	120	
Pro	Gln	Lys	Leu	Ala	Phe	Ala	Glu	Cys	Leu	Cys	Arg	Gly	Cys	Ile	125	130	135	
Asp	Ala	Arg	Thr	Gly	Arg	Glu	Thr	Ala	Ala	Leu	Asn	Ser	Val	Arg	140	145	150	
Leu	Leu	Gln	Ser	Leu	Leu	Val	Leu	Arg	Arg	Arg	Pro	Cys	Ser	Arg	155	160	165	
Asp	Gly	Ser	Gly	Leu	Pro	Thr	Pro	Gly	Ala	Phe	Ala	Phe	His	Thr	170	175	180	
Glu	Phe	Ile	His	Val	Pro	Val	Gly	Cys	Thr	Cys	Val	Leu	Pro	Arg	185	190	195	
Ser	Val														197			

FIGURE 3

gccagggtgtg caggccgctc caagcccagc ctgccccgct gccgccacca 50
tgacgctcct ccccggcctc ctgtttctga cctggctgca cacatgcttg 100
gcccaccatg acccctccct cagggggcac ccccacagtc acggtacccc 150
aactgctac tcggctgagg aactgcccct cggccaggcc cccccacacc 200
tgctggctcg aggtgccaaag tgggggcagg ctttgccctgt agccctgggtg 250
tccagcctgg aggcagcaag ccacaggggg aggcacgaga ggccctcagc 300
tacgaccag tgcccgggtgc tgcggccgga ggaggtggtg gaggcagaca 350
cccaccagcg ctccatctca ccctggagat accgtgtgga cacggatgag 400
gaccgctatc cacagaagct ggccttcgcc gagtgcctgt gcagaggctg 450
tategatgca cggacggggc gcgagacagc tgcgctcaac tccgtgcggc 500
tgctccagag cctgctgggtg ctgcgccgcc ggccctgctc ccgcgacggc 550
tcggggctcc ccacacctgg ggcctttgcc ttccacaccg agttcatcca 600
cgteccccgtc ggetgcacct gcgtgctgcc ccgttcagtg tgaccgccga 650
ggccgtgggg cccctagact ggacacgtgt gctccccaga gggcaccccc 700
tatttatgtg tatttattgt tatttatatg cctcccccaa cactaccctt 750
ggggtctggg cattccccgt gtctggagga cagcccccca ctgttctcct 800
catctccagc ctcagtagtt gggggtagaa ggagctcagc acctcttcca 850
gcccttaaag ctgcagaaaa ggtgtcacac ggctgcctgt accttggtc 900
cctgtcctgc tcccggcttc ccttacccta tcaactggcct caggccccgc 950
aggctgcctc ttcccaacct ccttgaagt acccctgttt cttaaacaat 1000
tatttaagtg tacgtgtatt attaaactga tgaacacatc cccaaaa 1047

FIGURE 4

ggcagcaggg accaagagag gcacgcttgc ccttttatga catcagagct 50
 cctgggttctt gctccttggg actctgggac ttacaccagt ggcacccctg 100
 gctcnnnnnn nnnnnaattc ggtacgaggc tgggggttcag gcgggcagca 150
 gctgcaggct gaccttgcag cttggcgga tggactggcc tcacaacctg 200
 ctgtttcttc ttaccatttc catcttcctg gggctgggcc agcccaggag 250
 ccccaaaagc aagaggaagg ggcaagggcg gcctgggccc ctggtccttg 300
 gccctcacca ggtgccactg gacctggtgt cacggatgaa accgtatgcc 350
 cgcatggagg agtatgagag gaacatcgag gagatgttgg ccagctgag 400
 gaacagttca gagctggccc agagaaagtg tgaggtcaac ttgcagctgt 450
 ggatgtccaa caagaggagc ctgtctccct ggggctacag catcaaccac 500
 gaccccagcc gtatccccgt ggacctccgg aggcacggtg cctgtgtctg 550
 ggcttgtgtg aacccttca ccatgcagga ggaccgcagc atggtgagcg 600
 tgccggtgtt cagccagggt cctgtgcgcc gccgcctctg ccgccaccg 650
 cccgcacag ggccttgccg ccagcgcgca gtcatggaga ccatcgctgt 700
 gggctgcacc tgcattctct gaatcgacct ggcccagaag ccaggccagc 750
 agcccagagac catcctcctt gcacctttgt gccaaagaag gcctatgaaa 800
 agtaaacact gacttttgaa agcaaaaaaa 830

FIGURE 5

FIGURE 7A

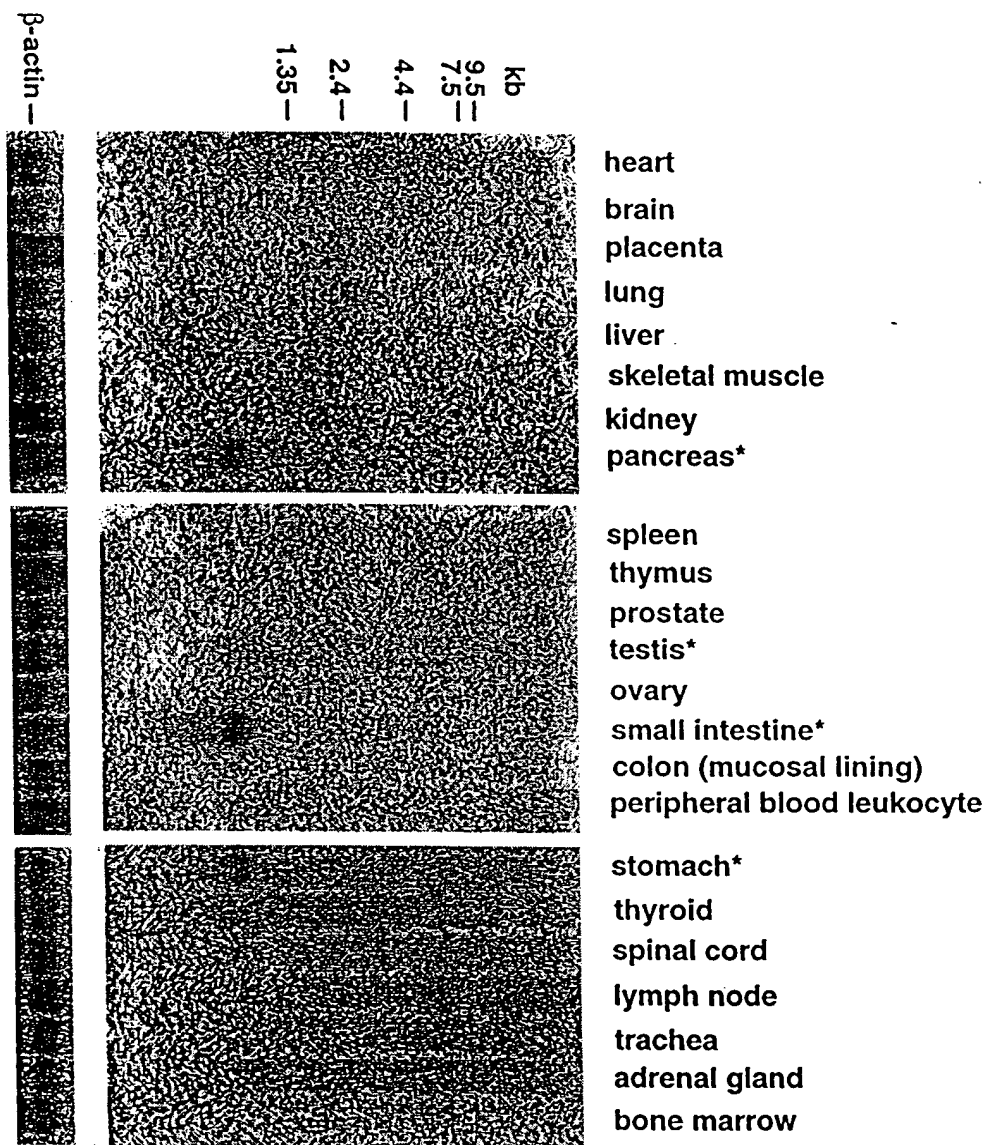
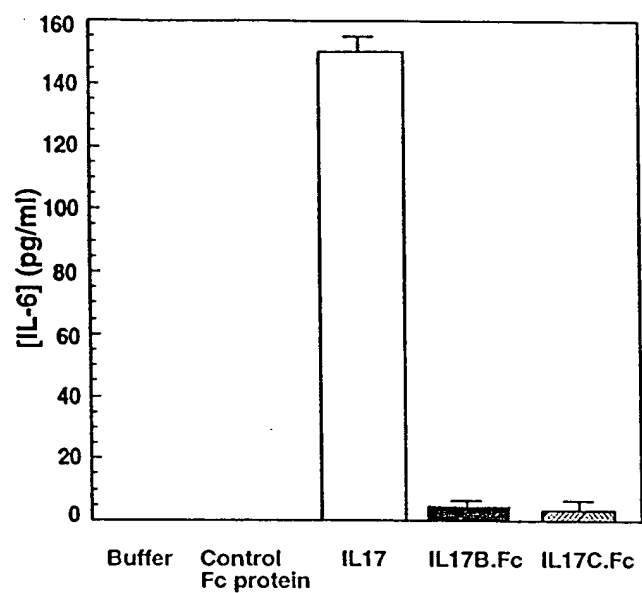


FIGURE 8

A. HFF cells



B. THP1 cells

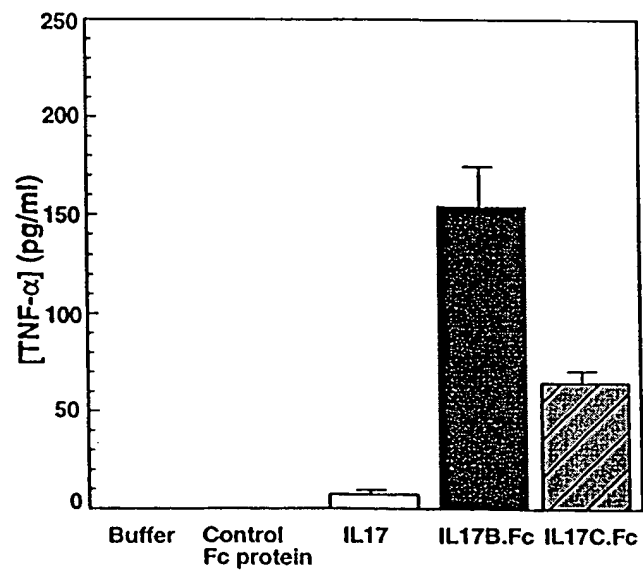
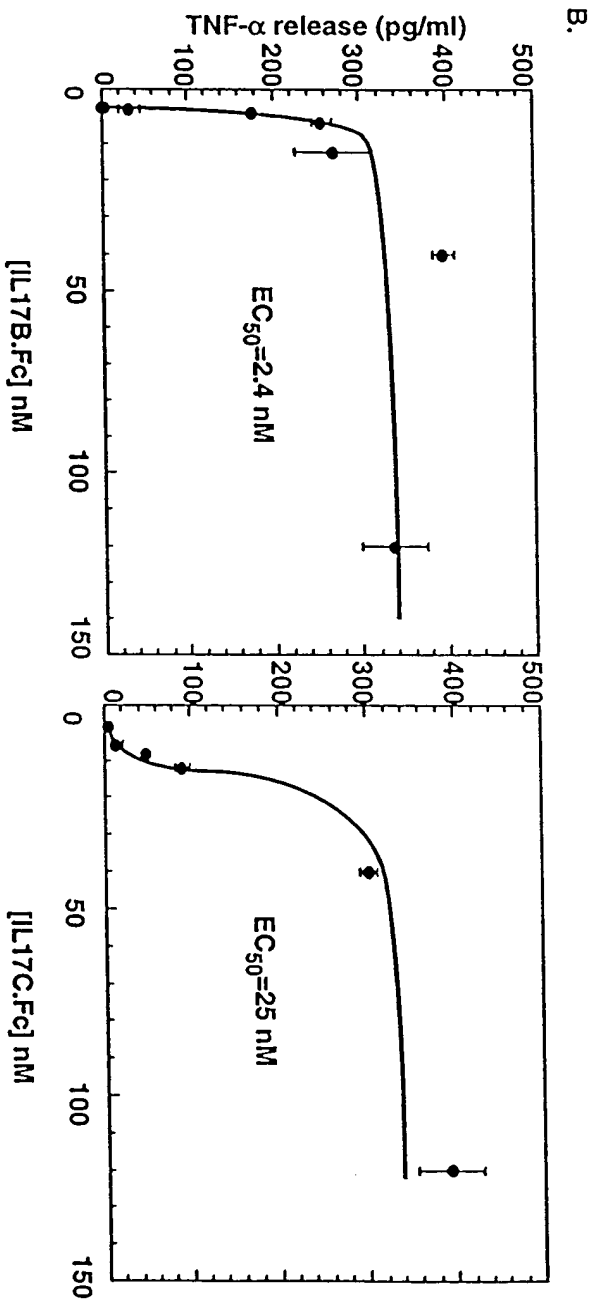
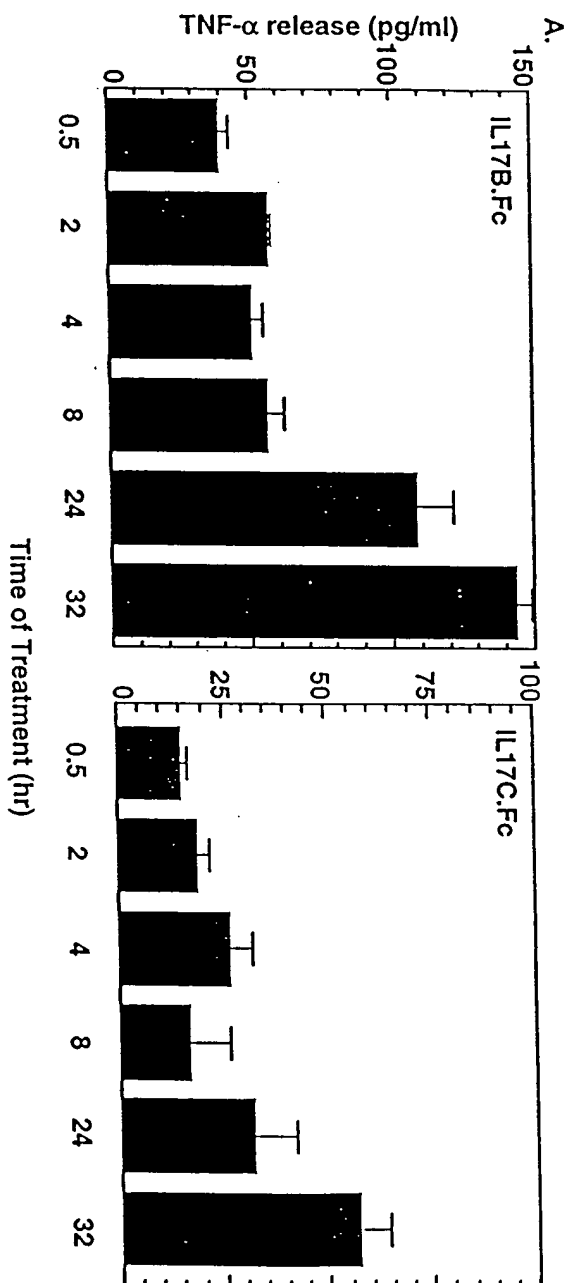


FIGURE 9

FIGURE 10



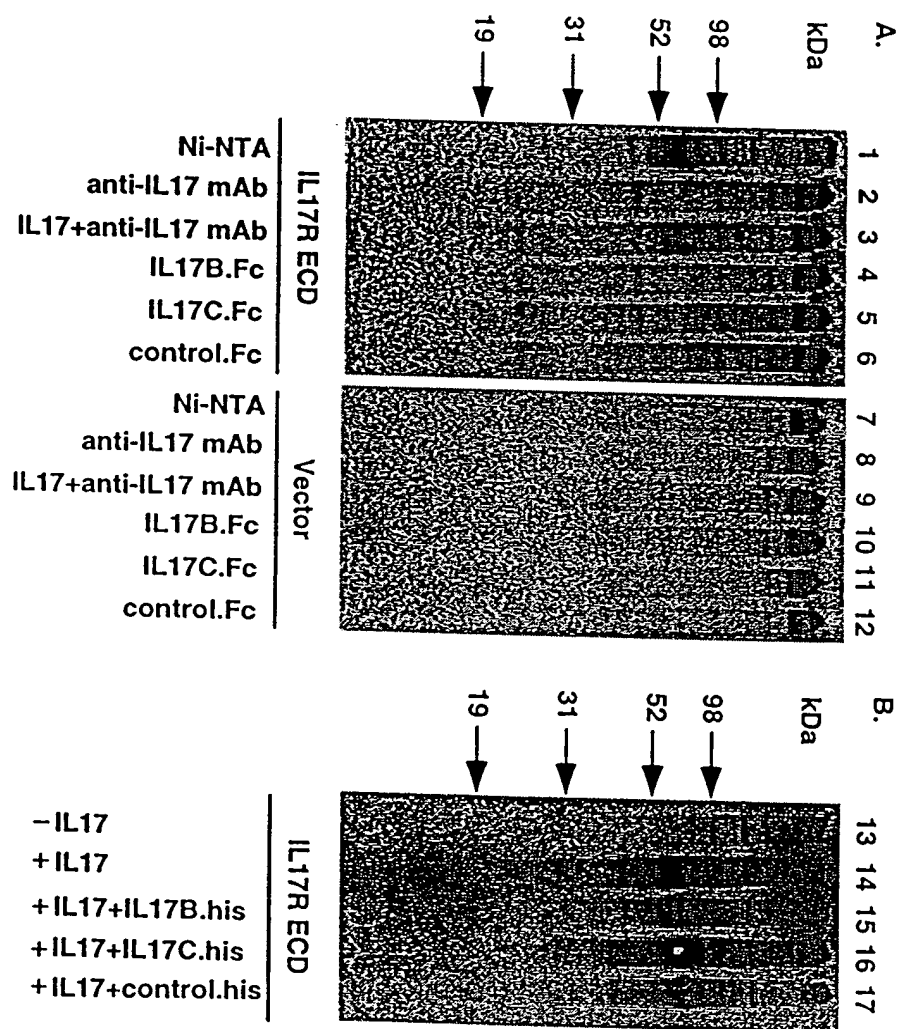


FIGURE 11

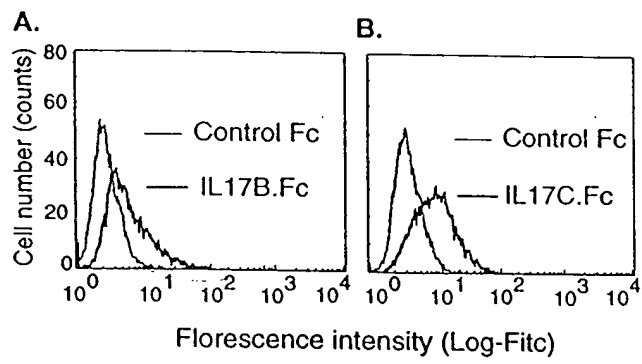


FIGURE 12

IL-17 induces breakdown and inhibits synthesis of cartilage matrix

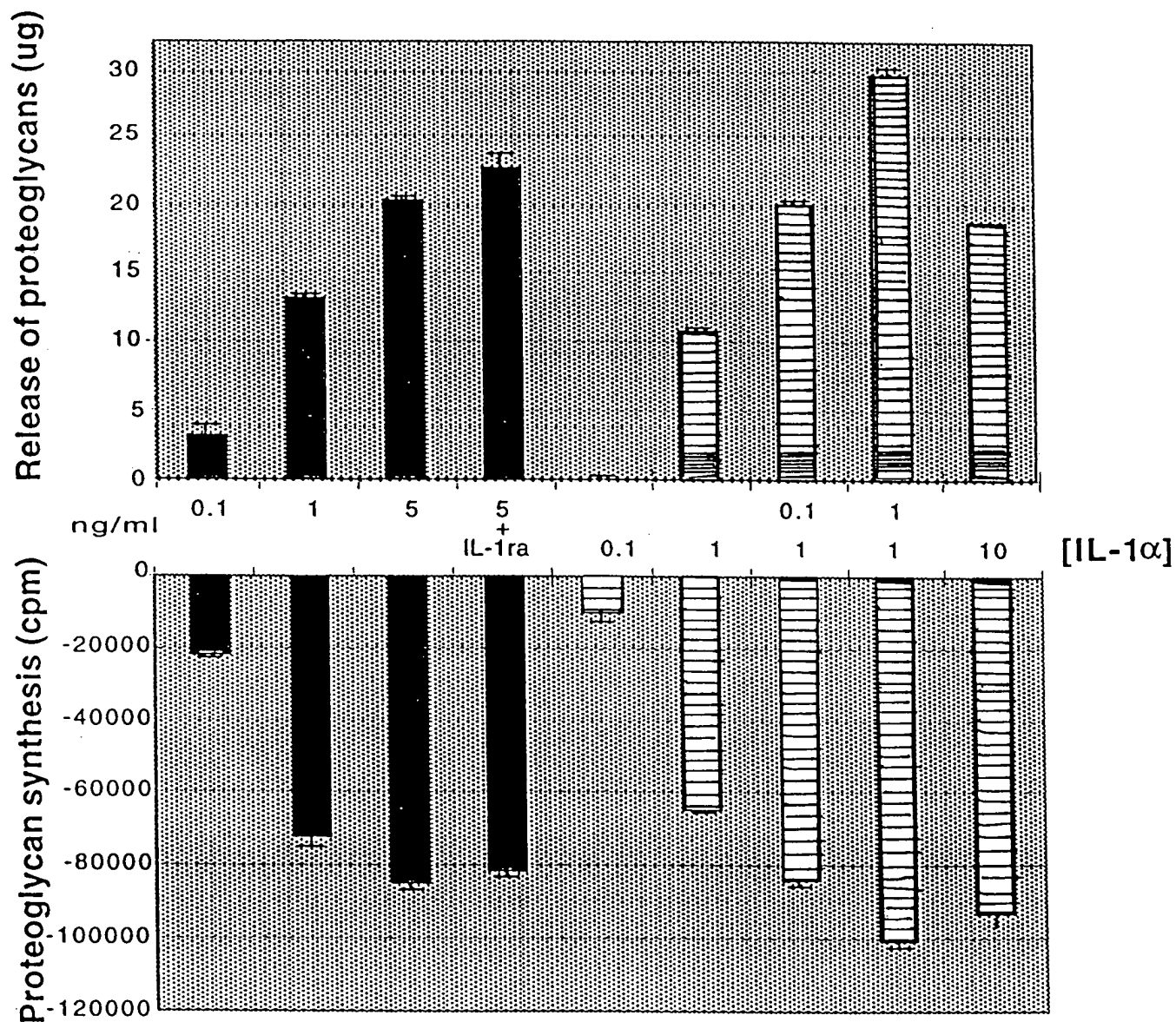


FIGURE 13

IL 17 increases basal and
IL-1 α -induced nitric oxide release

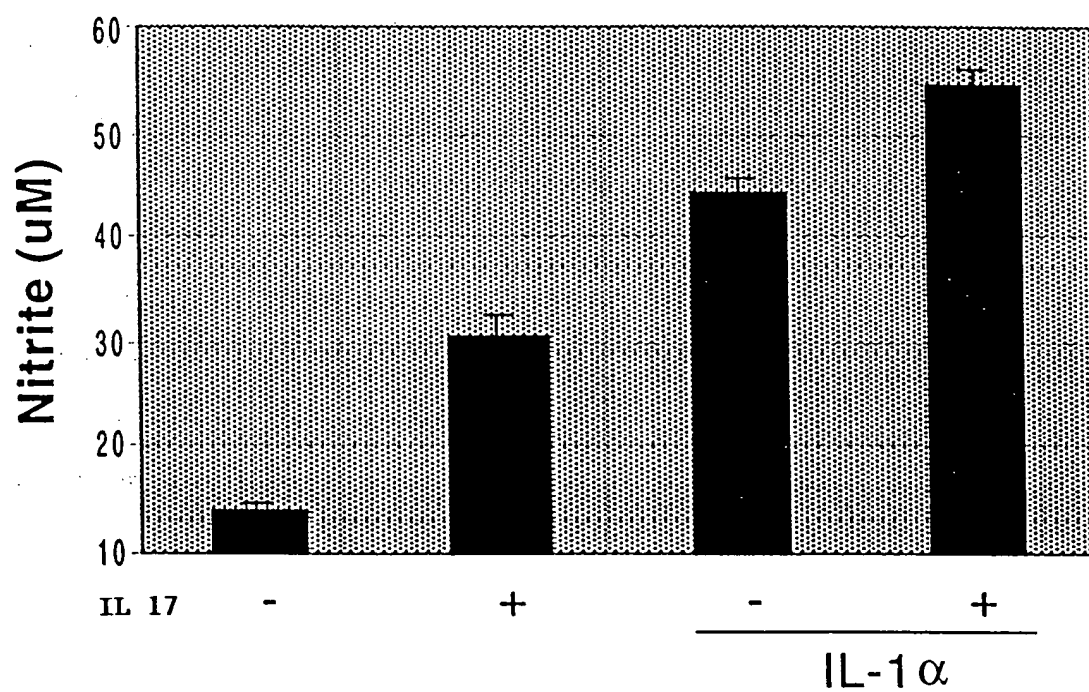
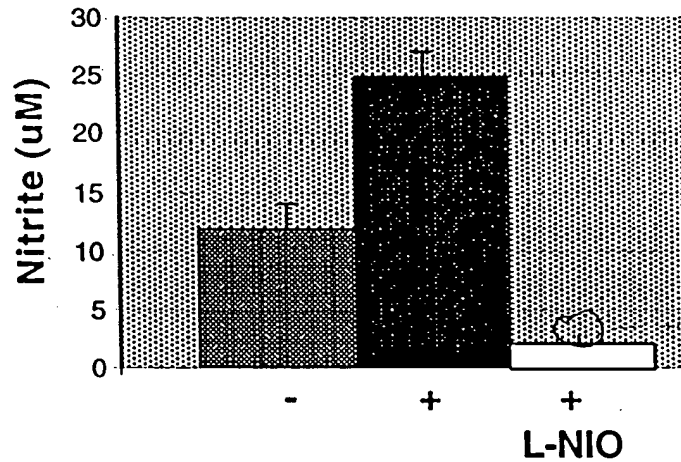


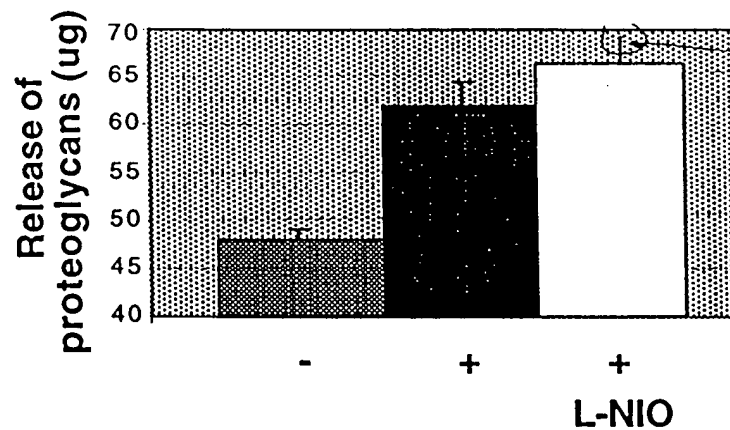
FIGURE 14

Inhibition of nitric oxide release does not block the detrimental effects of IL 17 on matrix breakdown or synthesis

A.



B.



C.

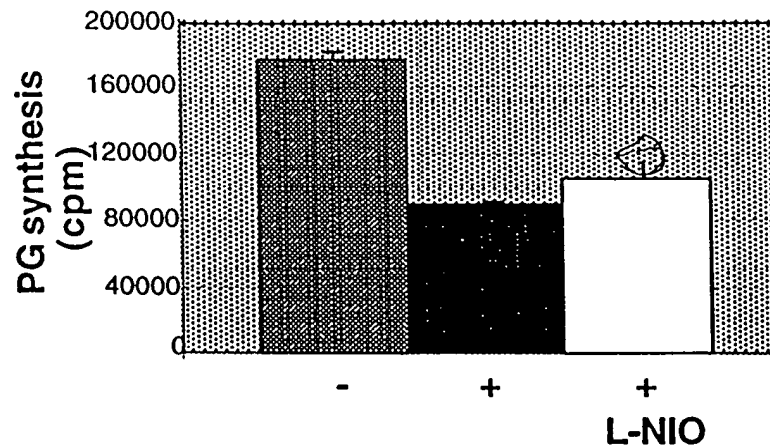


FIGURE 15

INHIBITION of NO release enhances
 IL1- α -induced matrix breakdown
 but not matrix synthesis

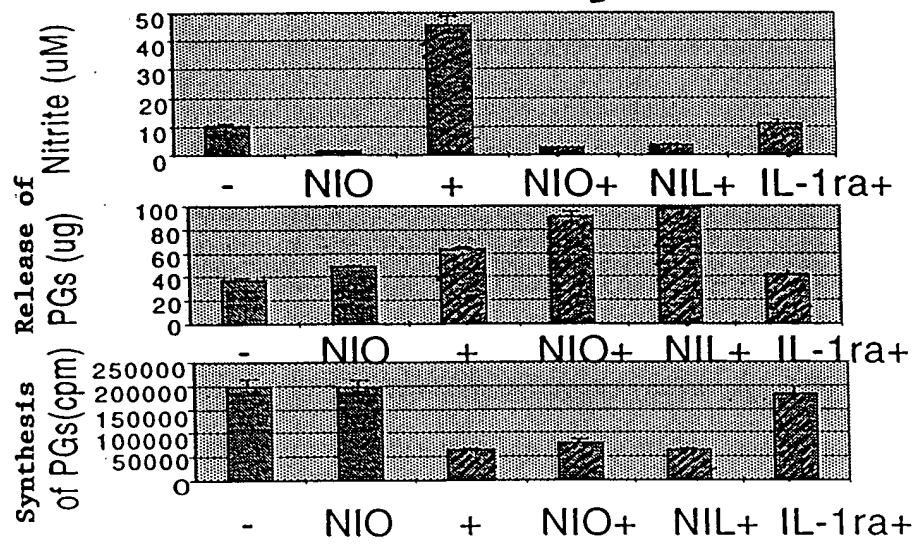


FIGURE 16

IL 17 homologue 1 (UNQ516)
has positive effects on
articular cartilage

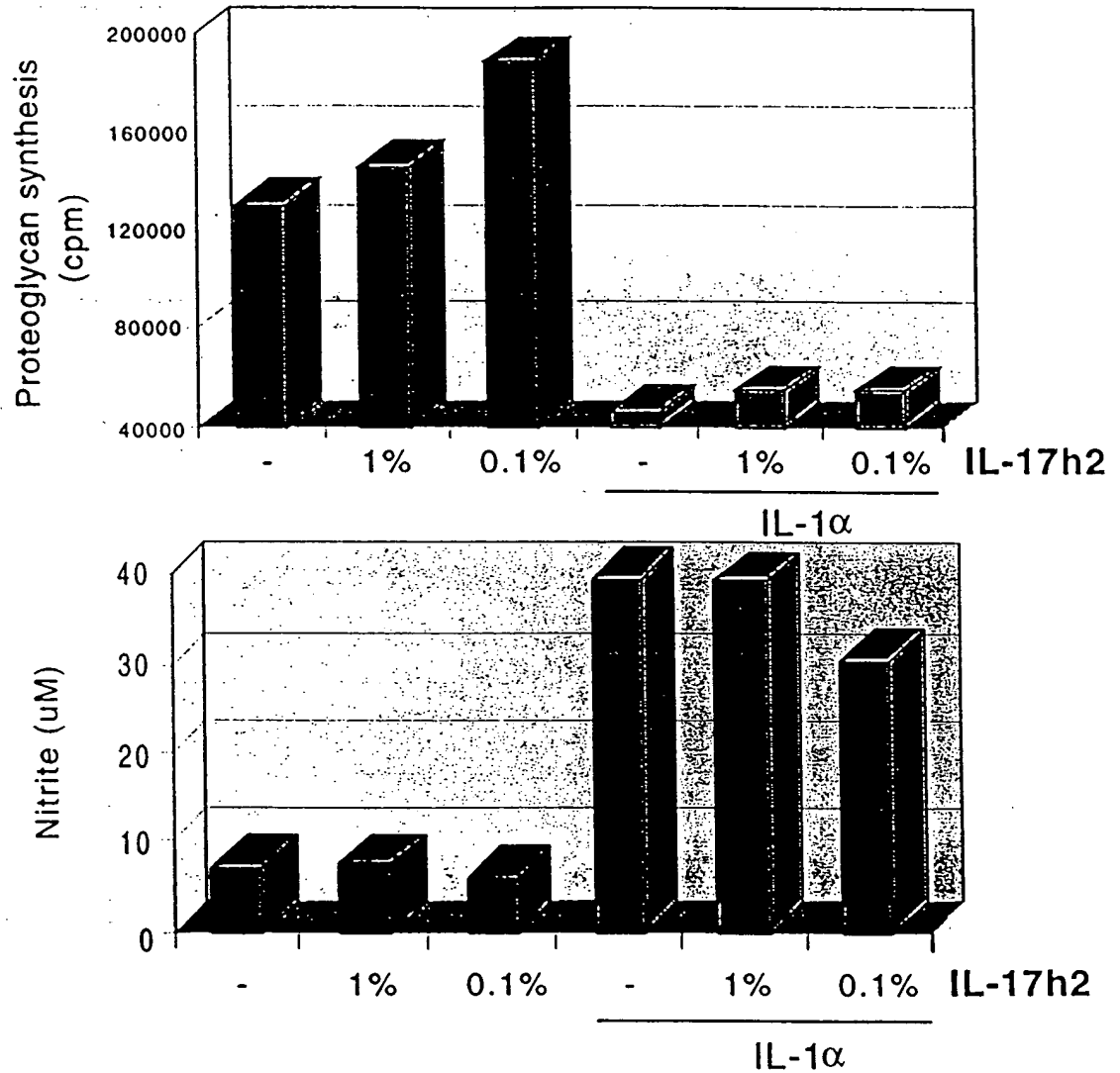


FIGURE 17

IL 17 homologue (UNQ 561) has detrimental effects on articular cartilage

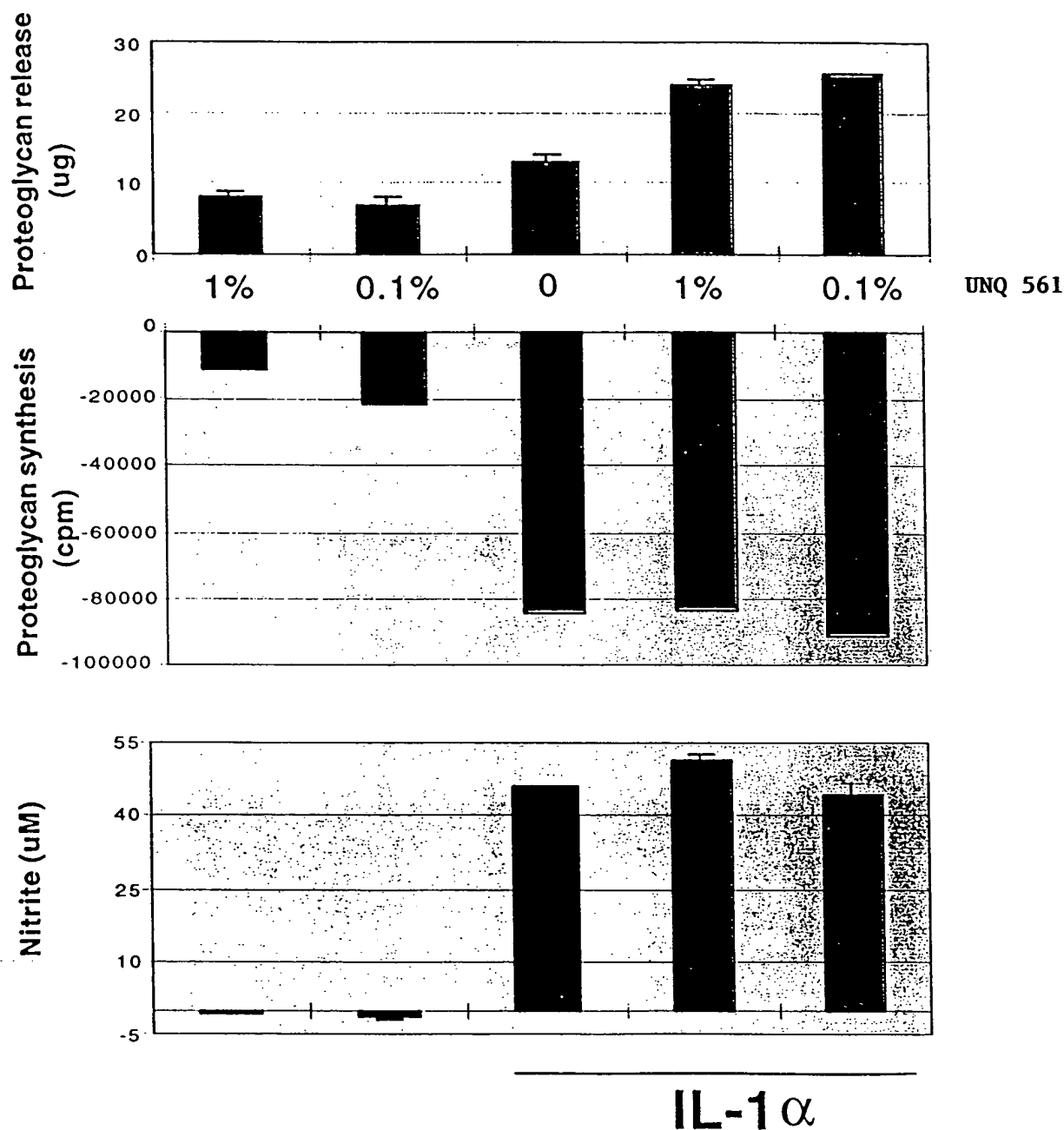


FIGURE 18